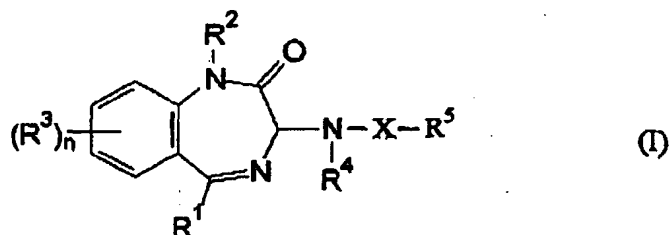


CLAIMS

1. Use of a compound which is (a) a benzodiazepine derivative of the formula  
(I) or an N-oxide thereof or (b) a pharmaceutically acceptable salt thereof, in the  
5 manufacture of a medicament for use in treating or preventing an RSV infection

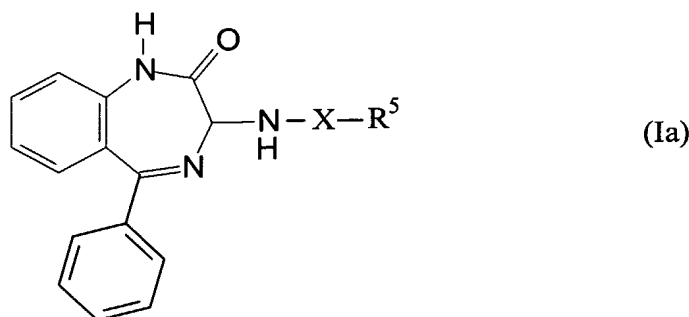


wherein:

- R¹ represents C<sub>1-6</sub> alkyl, aryl or heteroaryl;
- 10 - R² represents hydrogen or C<sub>1-6</sub> alkyl;
- each R³ is the same or different and represents halogen, hydroxy, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> haloalkyl, C<sub>1-6</sub> haloalkoxy, amino, mono(C<sub>1-6</sub> alkyl)amino, di(C<sub>1-6</sub> alkyl)amino, nitro, cyano, -CO<sub>2</sub>R', -CONR'R'', -NH-CO-R', -S(O)R', -S(O)<sub>2</sub>R', -NH-S(O)<sub>2</sub>R', -S(O)NR'R'' or -S(O)<sub>2</sub>NR'R'', wherein each R' and  
15 R'' is the same or different and represents hydrogen or C<sub>1-6</sub> alkyl;
- n is from 0 to 3;
- R⁴ represents hydrogen or C<sub>1-6</sub> alkyl;
- X represents -CO-, -CO-NR', -S(O)- or -S(O)<sub>2</sub>-, wherein R' is hydrogen or a C<sub>1</sub>-C<sub>6</sub> alkyl group; and
- 20 - R⁵ represents an aryl, heteroaryl or heterocyclyl group, which group is substituted by a C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl group or a -(C<sub>1</sub>-C<sub>4</sub> alkyl)-X<sub>1</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl)-X<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) group, wherein X<sub>1</sub> represents -O-, -S- or -NR', wherein R' represents H or a C<sub>1</sub>-C<sub>4</sub> alkyl group and X<sub>2</sub> represents -CO-, -SO- or -SO<sub>2</sub>-, or R<sub>5</sub> represents -A<sub>1</sub>-Y-A<sub>2</sub>, wherein:
- 25 - A<sub>1</sub> is an aryl, heteroaryl, carbocyclyl or heterocyclyl group;
- Y represents a direct bond or a C<sub>1</sub>-C<sub>4</sub> alkylene, -SO<sub>2</sub>-, -CO-, -O-, -S- or -NR'-moiety, wherein R' is a C<sub>1</sub>-C<sub>6</sub> alkyl group; and

- A<sub>2</sub> is an aryl, heteroaryl, carbocyclyl or heterocyclyl group.
2. Use according to claim 1, wherein R<sup>1</sup> is C<sub>1-2</sub> alkyl or phenyl.
- 5 3. Use according to claim 1 or 2, wherein R<sup>2</sup> is hydrogen.
4. Use according to any one of the preceding claims wherein R<sup>3</sup> is halogen, hydroxy, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C<sub>1-4</sub> alkylthio, C<sub>1-4</sub> haloalkyl, C<sub>1-4</sub> haloalkoxy, amino, mono(C<sub>1-4</sub> alkyl)amino or di(C<sub>1-4</sub> alkyl)amino.
- 10 5. Use according to claim 4, wherein R<sup>3</sup> is fluorine, chlorine, bromine, C<sub>1-2</sub> alkyl, C<sub>1-2</sub> alkoxy, C<sub>1-2</sub> alkylthio, C<sub>1-2</sub> haloalkyl, C<sub>1-2</sub> haloalkoxy, amino, mono(C<sub>1-2</sub> alkyl)amino or di (C<sub>1-2</sub> alkyl)amino.
- 15 6. Use according to any one of the preceding claims wherein R<sup>4</sup> is hydrogen or C<sub>1-2</sub> alkyl.
7. Use according to any one of the preceding claims wherein X is -CO- or -CO-NR' - wherein R' represents hydrogen or a C<sub>1-2</sub> alkyl group.
- 20 8. Use according to any one of the preceding claims, wherein R<sup>5</sup> is a 5- or 6-membered heterocyclyl or heteroaryl ring which is substituted by a C<sub>1-6</sub> hydroxyalkyl group or a -(C<sub>1-4</sub> alkyl)-X<sub>1</sub>-(C<sub>1-4</sub> alkyl)-X<sub>2</sub>-(C<sub>1-4</sub> alkyl) group, wherein X<sub>1</sub> and X<sub>2</sub> are as defined in claim 1.
- 25 9. Use according to claim 8, wherein R<sup>5</sup> is a 5- or 6- membered heteroaryl group which is substituted by a -CH<sub>2</sub>-OH or -(C<sub>1-4</sub> alkyl)-NR'-(C<sub>1-4</sub> alkyl)-S(O)<sub>2</sub>-(C<sub>1-4</sub> alkyl) substituent, wherein R' is hydrogen or C<sub>1-2</sub> alkyl.
- 30 10. Use according to any one of the preceding claims, wherein A<sub>1</sub> is an aryl or heteroaryl group.

11. Use according to claim 10, wherein A<sub>1</sub> is a phenyl group, a monocyclic 5- or 6- membered heteroaryl group or a 5- to 6- membered heteroaryl group fused to a monocyclic oxo-substituted 5- to 6- membered heterocyclyl group.
- 5 12. Use according to any one of the preceding claims wherein A<sub>1</sub> is unsubstituted or substituted by 1 or 2 substituents selected from halogen, cyano, nitro, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl and C<sub>1</sub>-C<sub>4</sub> alkoxy substituents.
- 10 13. Use according to any one of the preceding claims, wherein Y represents a direct bond, a C<sub>1</sub>-C<sub>2</sub> alkylene group, -SO<sub>2</sub>- or -O-.
14. Use according to any one of the preceding claims, wherein A<sub>2</sub> is a phenyl, 5- to 6- membered heteroaryl, 5- to 6- membered heterocyclyl or C<sub>3</sub>-C<sub>6</sub> cycloalkyl group.
- 15 15. Use according to any one of the preceding claims, wherein when A<sub>2</sub> is a heterocyclyl group it is attached to the moiety Y via a N atom.
16. Use according to any one of the preceding claims, wherein A<sub>2</sub> is unsubstituted or is substituted by 1 or 2 substituents which are selected from C<sub>1</sub>-C<sub>4</sub> alkyl and halogen substituents when A<sub>2</sub> is a heteroaryl or aryl group and which are selected from C<sub>1</sub>-C<sub>4</sub> alkyl, halogen and oxo substituents when A<sub>2</sub> is a carbocyclic or heterocyclyl group.
- 20 17. Use according to any one of the preceding claims, wherein A<sub>2</sub> is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or substituted by a C<sub>1</sub>-C<sub>2</sub> alkyl group.
- 25 18. Use according to any one of the preceding claims wherein the benzodiazepine derivative of formula (I) is a benzodiazepine derivative of formula (Ia):
- 30



wherein:

- X is -CO- or -CO-NH- ; and
- 5 - R<sup>5</sup> is a 5- to 6- membered heteroaryl group, for example a furanyl group, which is substituted by -CH<sub>2</sub>-OH or -(C<sub>1</sub>-C<sub>4</sub> alkyl)-N(CH<sub>3</sub>)-(C<sub>1</sub>-C<sub>4</sub> alkyl)-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) or R<sub>5</sub> represents -A<sub>1</sub>-Y-A<sub>2</sub>, wherein:
  - A<sub>1</sub> is a phenyl, pyridyl, furanyl, thiazolyl, oxazolyl, isoxazolyl, thienyl or 1H-imidazo[4,5-b]pyridin-2-(3H)-one moiety, which is unsubstituted or substituted
  - 10 by 1 or 2 substituents selected from halogen, cyano, C<sub>1</sub>-C<sub>2</sub> alkyl, C<sub>1</sub>-C<sub>2</sub> haloalkyl and C<sub>1</sub>-C<sub>2</sub> alkoxy substituents;
  - Y is a direct bond, a C<sub>1</sub>-C<sub>2</sub> alkylene group, -SO<sub>2</sub>- or -O-; and
  - A<sub>2</sub> is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or
  - 15 substituted by a C<sub>1</sub>-C<sub>2</sub> alkyl group.

19. Use according to any one of the preceding claims, wherein the medicament is for use in treating a patient who is a child under two years of age, an adult suffering from asthma, chronic obstructive pulmonary disorder (COPD) or immunodeficiency,

20 an elderly person or a person in a long term care facility.

20. Use according to claim 19 wherein said child suffers from chronic lung disease.

21. Use according to any one of claims 1 to 18 wherein the medicament is for use in preventing RSV infection in an infant less than six years of age who was born after 32 weeks of gestation or less.

22. Use according to any one of the preceding claims, wherein the medicament is suitable for intranasal or intrabronchial administration.
- 5 23. Use according to any one of the preceding claims, wherein the medicament further comprises an anti-inflammatory compound or an anti-influenza compound.
24. Use according to claim 23 wherein the anti-inflammatory compound is budesonide or fluticasone.
- 10 25. Use according to claim 23 wherein the anti-inflammatory compound is a leukotriene antagonist, phosphodiesterase 4 inhibitor or TNF alpha inhibitor.
26. Use according to claim 23 wherein the anti-inflammatory compound is an  
15 interleukin 8 or interleukin 9 inhibitor.
27. Use according to any one of claims 1 to 22 wherein the medicament is coadministered with an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an anti-influenza compound.
- 20 28. A method of treating a patient suffering from or susceptible to an RSV infection, which method comprises administering to said patient an effective amount of a compound as defined in any one of claims 1 to 18.
- 25 29. A method according to claim 28, wherein said patient is a patient as defined in any one of claims 19 to 21.
30. A method according to claim 28 or 29, wherein said compound is administered intranasally or intrabronchially.
- 30 31. An inhaler or nebuliser containing a medicament which comprises  
(a) a compound as defined in any one of claims 1 to 18, and

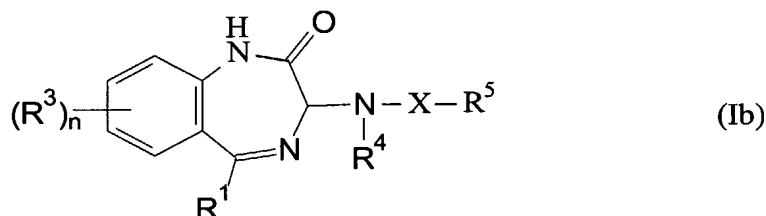
(b) a pharmaceutically acceptable carrier or diluent.

32. A product comprising a compound as defined in any one of claims 1 to 18  
and an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an  
5 anti-influenza compound.

33. Use of a product according to claim 32 in the manufacture of a medicament  
for use in the treatment of concomitant RSV and influenza infections.

10 34. Use of a compound as defined in any one of claims 1 to 18 in the  
manufacture of a medicament for use in the treatment of human metapneumovirus,  
measles, parainfluenza viruses, mumps, yellow fever virus (B5 strain), Dengue 2  
virus or West Nile virus.

15 35. A compound which is (a) a benzodiazepine derivative of formula (Ib) or an  
N-oxide thereof, or (b) a pharmaceutically acceptable salt thereof



20 wherein  $R_1$ ,  $R_3$ ,  $n$ ,  $R_4$ ,  $X$  and  $R_5$  are as defined in any one of claims 1 to 18.

36. A compound according to claim 35, wherein  $R_1$  is an unsubstituted phenyl  
group.

25 37. A compound according to claim 35 or 36, wherein when  $A_1$  is a heteroaryl  
group, it is other than a 5-methyl-isoxazolyl moiety.

38. A compound according to any one of claims 35 to 37, wherein  $A_1$  is an aryl  
or heteroaryl moiety.

39. A compound according to any one of claims 35 to 38, wherein X is -CO- or -CO-NR', wherein R' is as defined in any one of claims 1 to 18, provided that when X is -CO-NR', the moiety -A<sub>1</sub>-Y-A<sub>2</sub> is -phenyl-O-phenyl.

5

40. A compound according to any one of claims 35 to 39, wherein A<sub>2</sub> is other than a 4- to 10- membered saturated cycloalkyl ring, in which one of the carbon atoms is replaced by a N atom.

10 41. A compound according to any one of claims 35 to 40, wherein A<sub>2</sub> is a piperazinyl, pyridyl, pyrrolidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group which is unsubstituted or is substituted by a C<sub>1</sub>-C<sub>2</sub> alkyl group.

42. A compound according to claim 35, wherein the benzodiazepine derivative of  
15 the formula (Ib) is:

6-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;

3,4,5,6-Tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

20 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-Chloro-4-morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

25 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-fluoro-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-Chloro-2-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-5-fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

30 (S)-5-(4-Methyl-piperazin-1-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Pyrrolidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

- 1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 (S)-5-Piperidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 (S)-5-Dimethylaminomethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-  
 5 1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 (S)-4-Fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-benzamide;  
 (S)-4-Fluoro-2-morpholino-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
 10 (S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-benzamide;  
 (S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-piperidine-1-yl-benzamide;  
 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-  
 15 yl-4-trifluoromethyl-benzamide;  
 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-4-trifluoromethyl-benzamide;  
 (S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-4-trifluoromethyl-benzamide;  
 20 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-5-trifluoromethyl-benzamide;  
 (S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-5-trifluoromethyl-benzamide;  
 (S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-  
 25 yl)-nicotinamide;  
 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;  
 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-3-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
 30 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-6-methyl-N-(2-oxo-5-phenyl-2,3-



- dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
(S)-2-Chloro-6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
(S)-3-Cyclopropyl-2-oxo-2,3-dihydro-imidazo[4,5-b]pyridine-1-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
5 (S)-3-(4-Methyl-piperazine-1-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
(S)-4-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
10 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(piperidine-1-sulfonyl)-benzamide;  
(S)-3-(Morpholine-4-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
(S)-5-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
15 (S)-5-Hydroxymethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
(S)-5-(1,1-Dioxo-1λ6-thiomorpholin-4-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
20 (S)-2-Chloro-4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
(S)-2-Chloro-5-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
(S)-5-([(2-Methanesulfonyl-ethyl)-methyl-amino]-methyl)-furan-2-carboxylic acid  
25 (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
(S)-2-Pyridin-3-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
(S)-2-Pyridin-4-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
30 (S)-4-Methyl-2-pyrazin-2-yl-thiazole-5-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
(S)-2-Morpholin-4-ylmethyl-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

- 1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 (S)-3-Morpholin-4-ylmethyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
 (S)-5-Morpholin-4-ylmethyl-isoxazole-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 5 (S)-3-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 (S)-5-Pyridin-2-yl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 10 (S)-2-Methyl-4-(morpholin-4-sulfonyl)-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 (S)-6-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;  
 (S)-3-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 15 (S)-5-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;  
 2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;  
 20 (S)-5-Phenyl-oxazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide; or  
 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxyphenyl)-urea.
- 25 43. A compound according to any one of claims 35 to 42 for use in a method of treating the human or animal body.
44. A pharmaceutical composition comprising a compound according to any one of claims 35 to 43, and a pharmaceutically acceptable diluant or carrier.
- 30 45. A composition according to claim 44 comprising an optically active isomer of a compound according to any one of claims 35 to 42.

46. A composition according to claim 44 or 45 which is in the form of a tablet, troche, lozenge, aqueous or oily suspension, dispersible powders or granules.